

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 24 September 1999 (24.09.99)	
International application No. PCT/US99/00419	Applicant's or agent's file reference 5368-PCT
International filing date (day/month/year) 08 January 1999 (08.01.99)	Priority date (day/month/year) 09 January 1998 (09.01.98)
Applicant PETTIT, George, R. et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

09 August 1999 (09.08.99)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Jean-Marie McAdams
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

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REC'D 23 MAY 2000

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 5368-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/00419	International filing date (day/month/year) 08 JANUARY 1999	Priority date (day/month/year) 09 JANUARY 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): C07F 9/09 and US Cl.: 558/197, 207, 210, 215		
Applicant ARIZONA BOARD OF REGENTS, A BODY CORPORATE, ACTING ON BEHALF OF ARIZONA STATE UNIVERSITY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 09 AUGUST 1999	Date of completion of this report 23 APRIL 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JEAN F. VOLLANO  Telephone No. (703) 308-1235

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/00419

I. Basis of the report

1. With regard to the elements of the international application:*

 the international application as originally filed the description:

pages 1-42

pages NONE

pages NONE

, filed with the letter of

 the claims:

pages 43-45

pages NONE

pages NONE

pages NONE

, filed with the letter of

 the drawings:

pages 1-2

pages NONE

pages NONE

, filed with the letter of

 the sequence listing part of the description:

pages NONE

pages NONE

pages NONE

, filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. The amendments have resulted in the cancellation of: the description, pages NONE the claims, Nos. NONE the drawings, sheets/fig NONE5. This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/00419

V. Reason d statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)

Claims	1-8	YES
Claims	9	NO

Inventive Step (IS)

Claims	1-8	YES
Claims	9	NO

Industrial Applicability (IA)

Claims	1-9	YES
Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-8 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the process for preparing combretastatin A-4 produgs and trans combretastatin A-prodrugs by the method found in the instant invention.

Claim 9 lacks an inventive step under PCT Article 33(3) as being obvious over Pettit et al (US 4,996,237) in view of Pettit (US 5,561,122).

Pettit et al teaches the known combretastatin A-4 compound as a useful compound which has biological activity (e.g., anti tumor activity).

Pettit et al teaches that the compound has a phenoxy (i.e., Ph-OH) moiety as part of its structure.

Pettit teaches that the useful compound is formulated as a combretastatin A-prodrug which includes a phosphonate group in place of the hydroxy portion of the molecule.

Pettit teaches that the phosphonate portion is a salt which includes Group 1 metals (e.g., sodium or potassium) or ammonia.

Pettit differs from the instant invention in that the salt is not a cesium salt.

However it would have been obvious to use any of the Group 1 metal salts as a prodrug salt with the expectation of having a prodrug with similar characteristics and properties as the compounds of Pettit, since Pettit teaches that the phosphonate salts of Group 1 are useful prodrug compounds.

Claims 1-9 meet the criteria set out in PCT Article 33(4), for industrial applicability.

----- NEW CITATIONS -----

NONE

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/00419

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C07F 9/09
 US CL :558/197, 207, 210, 215

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 558/197, 207, 210, 215

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,561,122 A (PETTIT) 01 October 1996 (01/10/96) see entire document, especially columns 1 and 2.	1-8
-		---
Y	Database CAPLUS on STN, Chem Abstracts, (Columbus OH, USA) No. 94:197470 , TANIGUCHI, M. et al. 'Study of phosphate esters as prodrugs. Part 3. Synthesis and evaluation in vitro of 4-acetamidophenyl phosphate.' Chem. Pharm. Bull. Abstract, February 1981, 29(2), 577-580.	9
Y	US 4,996,237 A (PETTIT et al.) 26 February 1991 (26/02/91) see entire document, especially examples.	9

Further documents are listed in the continuation of Box C. See patent family annex.

Special categories of cited documents:		
"A" document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"B" earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"A"	document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

02 MARCH 1999

Date of mailing of the international search report

24 MAR 1999

Name and mailing address of the ISA/US
 Commissioner of Patents and Trademarks
 Box PCT
 Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized Officer
D. Haunseuse Jr.
 JEAN F VOLLANO

Telephone No. (703) 308-1235

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/00419

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, CAS ONLINE, BEILSTEIN, GMELIN, CASREACT

search terms: phosphorylation, structure search, combrestatin, phosphate ester, prodrug, dibenzyl phosphite, diethylamido, phosphine, diisopropylamido phosphine, phenol